OPTIMIZATION OF DEVICE STRUCTURE AND LUMINANCE EMISSION PROFILES OF ORGANIC LIGHT-EMITTING DISPLAYS FOR MEDICAL IMAGING APPLICATIONS

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Advancements in organic polymer light-emitting devices and displays (OP-LED) during the past years have positioned this technology as a candidate for demanding applications, such as the diagnostic interpretation of digital mammography images. In our work, we developed simulation tools to study the optical performance of OP-LED with respect to efficiency, angular emission distribution, and display reflectance. We applied an optical Monte Carlo method for modeling the light transport phenomena OP-LEDs fabricated on plastic substrates. The OP-LED consists of a combination of a hole-transport layer and a light-emitting polymer layer. In this simulation, we assumed a point source with an emission spectrum given by the photoluminescence (PL) of organic polymers measured in our laboratories. This simulation describes the fate of photons through multiple scattering events, determined by the wavelength-dependent material optical properties in a three-dimensional Cartesian geometry, considering the effects of refraction, back-reflection, and absorption within the polymer layers. We used absorption coefficients measured by UV-visible absorption and photothermal deflection spectroscopy. The refractive indices were obtained by spectroscopic ellipsometry. First, we analyzed the spectral distribution and device extraction efficiency, and found that the simulated emission spectra of green and red light-emitting devices are similar to the measured PL spectra. We conclude that waveguiding cannot be neglected, and that its contribution depends on substrate thickness and refractive index. We further investigated the luminance angular distribution of OP-LEDs, and found that it follows a pseudo-Lambertian profile with increased intensity in the forward direction. Finally, we present a method based to calculate the bidirectional reflectance distribution function (BRDF) of emissive displays. We validated our results using simple models with known exact analytical solution, and experimental measurements. We conclude that for emissive display technologies, the reflections are slightly more forward-peaked than the predictions of Lambertian profiles. We show that the BRDF of OP-LEDs backed with a metallic reflective electrode is highly specular.

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RECENT ADVANCES IN THE APPLICATION OF DIFFRACTION ENHANCED IMAGING TO BREAST CANCER RESEARCH

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A number of x-ray imaging methods have introduced new contrast mechanisms to radiography in addition to absorption. The Diffraction Enhanced Imaging (DEI) technique has two additional contrast mechanisms, refraction gradient and ultra-small-angle scatter rejection (extinction), that have properties that are useful for soft tissue imaging as well as the potential to greatly reduce x-ray exposure.

Some recent results of the application and analysis of DEI for breast cancer imaging will be presented. Three new methods that extend the capability of the DEI technique by extracting new information and interpretation will be presented.

First, we have investigated the contrast mechanisms of the refraction angle, and the apparent absorption images obtained from DEI and have correlated them with the absorption contrast of conventional radiography for breast cancer specimens. We show that the density difference of fibrils in breast cancer as measured by absorption images correlate well with the density difference derived from refraction angle images of DEI. In addition we find that the DEI apparent absorption image and the image obtained with the DEI system at the top of the reflectivity curve have much greater contrast than that of the normal radiograph (x 8 to 33-fold higher). This is due to the rejection of small angle scattering (extinction) from the fibrils enhancing the contrast.

Second, we have shown that an improved data acquisition scheme and interpretation can lead to more information extraction from the DEI system that was possible from the two image DEI technique. This new approach has been utilized to investigate and to visualize other contrast mechanisms from the DEI system. New images to radiography have been presented in the form of an extinction (scatter-rejection) images and a scattering width images as well as a pure refraction angle and absorption images unaffected by extinction effects. This type of analysis could possibly lead to other visualizations based on combinations of these images (absorption, refraction angle, extinction, and scattering width) that may enhance the appearance of cancer in breast tissue images.

Third, we present a method using the DEI refraction angle image that creates a mass density image. We show that this image contains similar information to that of a conventional radiograph (absorption image). Since the refraction angle image is best taken at high x-ray energies compared to conventional radiography, the dose and compression may be greatly reduced while still obtaining good tissue density contrast. We present images of test objects, compare the sensitivity and x-ray exposure of the technique for soft tissue imaging with conventional radiography, and present results obtained with breast cancer specimens. Finally, an update on efforts to assess if DEI can be developed into a viable laboratory / clinical system will be discussed.

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OUTCOMES OF SCREENING MAMMOGRAPHY IN ELDERLY WOMEN

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Context: Women age 65 years and older comprise only 14% of the U.S. female population, but nearly half of breast cancer diagnosed annually, and over half of breast cancer mortality occurs in this age group, making breast cancer a leading cause of cancer mortality in elderly women. There has been little research addressing whether mammography is effective in decreasing breast cancer mortality, or in improving health outcomes in elderly women. The goal of this research is to determine at what age mammographic screening no longer provides worthwhile benefit to elderly women.

Objective: To evaluate differences in the use of screening mammography by age, and to evaluate difference in breast cancer tumor attributes including size and stage, differences in breast cancer treatments, and differences in breast cancer mortality, between women who were previously screened with mammography and women who were not.

Methods: The SEER-Medicare database is a collaborative effort of the National Cancer Institute, the SEER program, and the Health Care Financing Administration (HCFA) to create a large population-based source of information for cancer related epidemiologic and health services research. This database provides an opportunity to study the outcomes related to mammographic screening in elderly women. These data include demographic information, utilization of health care resources including physician visits, mammography, and breast cancer treatments, and information on co-morbidities, detailed tumor information such as size and stage, and cause of death information for persons diagnosed with incident cancer. The SEER Medicare data was obtained describing 38,000 women ages 66 and above diagnosed with breast cancer between 1991 and 1996, and a 5% age matched sample of controls, and is being used to evaluate the outlined objectives.

Results: At the Era of Hope meeting, we plan to describe age related differences in the utilization of screening mammography, and describe how the use of screening mammography has increased over time. We hope to present results describing differences in the stage of disease at diagnosis as it varies by the utilization (and intensity) of mammographic screening.

Conclusion: The outlined studies will provide information to women and their physicians about the potential benefit of performing screening mammography in elderly women, as well as the potential harm as it relates to false positive diagnosis and over diagnosis of disease that may have otherwise remained silent. The large size of these databases will allow the results to be generalizeable to most elderly women in this country.

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INCREASING MAMMOGRAPHIC BREAST DENSITY IN RESPONSE TO HORMONE REPLACEMENT THERAPY AND BREAST CANCER RISK

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HYPOTHESIS: Women who have an increase in mammographic density in response to HRT are at higher risk for developing breast cancer than those women who do not have a change in mammographic appearance in response to HRT.

Hormone replacement therapy (HRT) has numerous benefits, but its use is also associated with a small increased risk of developing breast cancer. Currently, it is not possible to predict which women using HRT are at increased risk of developing breast cancer. HRT is known to slow the normal involution of the breast and causes an increase in mammographic density in 17-73% of women. This effect is more common with use of estrogen with progestin compared to estrogen alone. Women with increased mammographic density are also known to be at increased risk for developing breast cancer. We therefore hypothesize that women who have an increase in mammographic density in response to HRT are at higher risk for developing breast cancer than those women who do not have a change in mammographic appearance in response to HRT.

The purpose of this case-control study is to determine if an increase in mammographic breast density in response to HRT is associated with an increased risk of breast cancer. Because increasing breast density and cancer risk are more strongly associated with the use of estrogen and progestin, HRT use in this study will be limited to patients using both estrogen and progestin. The project entails comparison of pre- and post-HRT mammograms for women undergoing hormone replacement therapy (HRT) who were diagnosed with breast cancer at our institution between 1990 and 2000 (expected n = 122). To date, we have reviewed 444 charts of women undergoing mastectomy; 52 were using HRT. Cases will be frequency matched by year of diagnosis with a control population of postmenopausal women undergoing HRT who had a mammogram at our institution during the same year who had not developed breast cancer (1:2, case: control). Patients will also be matched by age and time between pre- and post-HRT mammograms. Additional clinical data will be obtained for use in the analysis, including duration of menopause and body mass index. Change in breast density over time will be assessed using quantitative digital analysis to determine the percentage of the breast occupied by breast tissue. The reader will be blinded as to HRT and case-control status. Odds ratios will estimate the association between HRT-associated increase in breast density and risk of breast cancer.

It is anticipated that if an increase in mammographic density in response to HRT indicates an increased risk of breast cancer development, alternative treatment for menopausal symptoms or lower dose HRT may be indicated. Thus, mammography could be used as a predictor for those at increased risk of breast cancer from HRT use.

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ANALYSIS OF IMAGE CONTRAST USING DIFFRACTION-ENHANCED IMAGING

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The contrast of simple objects and calcifications in breast tissue has been obtained using diffraction enhanced imaging (DEI) and compared to conventional radiographic contrast. Lucite cylinders, nylon wires and breast tissue samples containing calcifications were imaged using 18 keV synchrotron radiation at the National Synchrotron Light Source (NSLS) at Brookhaven National Laboratory. The DEI images were obtained by placing a silicon analyzer crystal tuned to the [333] diffraction plane in the beam path between the sample and the detector. The images showed improved contrast when compared to normal radiographs obtained without the analyzer crystal. The comparison of DEI images to conventional radiographs requires a consistent definition of refraction and absorption contrast. The proposed definitions were then used to find the DEI gain (the ratio of the DEI contrast with respect to the conventional image contrast). The results presented here show that the DEI gain is consistently greater than one for various object sizes. Computer modeling of DEI images was also done in order to determine how DEI gain is affected by the spatial resolution of the digital detector. The model accurately predicts the experimental results and also shows that the DEI gain depends on object size, pixel size, and detector point spread function (PSF). For objects large compared to the pixel size, the gain is near one and increases with decreasing object size. In the regime where the object is approximately the size of a pixel, the gain can be as high as 100. For The gain value also increases for decreasing pixel sizes and PSFs. The results of this study indicate that the improved contrast from DEI may provide more information than conventional radiography. This in turn can lead to improvements in the early detection of breast cancer.

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DOSE REQUIREMENTS IN STEREOMAMMOGRAPHY

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There is an increasing interest in adjunct mammographic applications, such as dual-energy mammography, angiography, tomographic imaging, and stereomammography. Tomographic and stereomammographic imaging hold particular promise due to the commonly-held belief that the normal mammographic structure can obscure the detection of abnormalities. The choice of optimum acquisition parameters of stereomammographs is subject to debate. In this work, we investigate the appropriate choice of exposure required in mono- and stereomammography.

A mammographic contrast-detail phantom (RMI-180) was imaged at 60 kVp, but variable mAs (2-100 mAs), using a Hologic digital radiography detector. At each technique, 5 images were obtained. The images, after appropriate corrections for detector performance were displayed to 6 human observers, using a perceptually-linearized 24-bit color monitor. The images were displayed in shades of gray either monoscopically or stereoscopically at 56 Hz per eye. Crystal Eyes stereoscopic goggles were worn by the observer, whether or not stereoscopic images were being viewed. The human observers were instructed in scoring the phantom prior to the experiment. Sixty images were presented in a single session, randomly selected, but balanced in terms of mAs and stereoscopy. Images were presented with grayscale set to display each image with constant noise or constant contrast.

We hypothesized that the quantum noise visible in stereoscopic images would be averaged by the human observer visual-perceptual system. This hypothesis implies that object visibility in stereoscopically acquired images should be equivalent to object visibility in a single image acquired at twice the dose of the individual projections viewed stereoscopically. Our results indicate that this hypothesis is true for images with significant quantum noise and readers with good stereoscopic vision.

These results indicate that in digital mammography, a stereoscopic image pair can be obtained with a total dose that is approximately equal to a single monoscopic image. The implication is that stereomammographic screening is achievable in terms of dose, but the practical issues of acquiring, displaying and storing twice as many images still needs to be addressed.

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3-DIMENSIONAL IMAGING OF THE BREAST

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We have investigated a variety of methods of imaging the breast in 3-D. Initially, we developed a method to determine the 3-D orientation and morphology of breast calcifications. This method uses an automated technique for performing limited-view, binary image reconstruction. In clinical trials, it has been shown to distinguish between preferentially peripherally distributed calcifications (predominantly benign) and homogeneously distributed calcifications (predominantly malignant). It is also able to elucidate the linear distribution of calcifications contained within the ductal system.

In order to image non-calcified tissues, and to relate calcifications to the surrounding tissue, we sought to compare alternative methods of generating 3-D images of the breast, namely stereoscopy, linear tomosynthesis, limited-view image reconstruction using algebraic reconstruction techniques, and micro-CT. Such methods are in theory capable of producing 3-D images of both calcifications and the surrounding breast tissue.

We have developed an imaging system that is capable of acquiring each of the images required for the different techniques. We have shown that stereoscopy has value in providing depth perception of tissues with little additional dose; however, often the small angle separating the views is insufficient to completely determine the causes of superposition. Tomosynthesis requires more views and potentially a higher dose, but provides better separation of tissues. Artifacts from the reconstruction algorithms can blur synthetic tomograms. CT, while providing the best 3-D images appears to require a dose that is not clinically acceptable. Final results of the limited-view reconstruction development program and clinical trial will be presented.

It is our purpose to develop a 3-D imaging method that will be clinically viable in terms of dose, image quality and equipment cost. We believe that these proposed developments will further enhance the 3-D imaging and evaluation of breast cancer by allowing the radiologist to view calcifications in relation to the surrounding tissue, and to allow 3-D imaging of non-calcified breast tissues at doses which are clinically acceptable.

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A NOVEL METHOD FOR THE DETERMINATION OF CALCIFICATION COMPOSITION

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Breast calcifications are one of the primary markers of both benign and malignant diseases in mammograms. However, little is known of their composition or the association of calcifications of specific composition with specific diseases. A method is under development to elucidate this relationship and allow differential diagnosis of calcifications in vivo.

Calcifications can be divided into two broad categories. Type I are crystalline, macroscopic microcalcifications. They are birefringent under polarized light. Elemental analysis shows them to be completely lacking phosphorous. X-ray diffraction of these monocrystals has shown them to be weddellite (calcium oxalate dihydrate). Type II are noncrystalline, macroscopic microcalcifications, which are generally larger than type I. Elemental analysis indicates that all type II calcifications have some phosphorus content, most typically as calcium hydroxyapatite.

Several investigators have shown that type I calcifications indicate either benign lesions or lobular hyperplasia. Type I microcalcifications are most frequently seen in benign microcysts, especially those with apocrine epithelium, and in dilated ducts. Type II calcifications are known to be associated with carcinoma. The presence of phosphorus in calcifications is believed to indicate rapid growth in a micromilieu containing phosphorus, such as necrotic detritus. It is generally accepted that the exclusive finding of type I calcifications is indicative of benign lesions. We propose to develop a technique that will determine the composition of calcifications prior to biopsy, thereby allowing one to avoid biopsy on Type I calcifications entirely, if so desired.

We believe that coherent scatter imaging (which is similar to x-ray diffraction imaging) may be the best way to determine the chemical composition of calcifications. We have demonstrated in proof-of-principle that we can discern different types of calcifications using this method. Extensive optimization and a dedicated detector design is ongoing.

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A METHOD FOR PRODUCING SIMULATED MAMMOGRAMS

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This project is to facilitate research in digital mammography and related technologies, in particular computer-aided diagnosis and image processing. A major limitation to the rapid development and subsequent clinical implementation of these technologies is the lack of a standardized set of mammograms to be used in development and evaluation.

We are developing a method to produce computer-simulated mammograms. Our approach is to use a computer model of image formation that predicts the appearance of an image based on an input x-ray distribution. The transfer of energy through the x-ray detector is modeled as a series of cascaded stochastic processes assuming that the x-ray phosphor consists of many thin phosphor layers. This model has been shown to predict accurately measures of image quality (spatial resolution and noise) for actual x-ray detectors. To obtain the distribution of x rays exiting the breast, we are acquiring high fidelity images of biopsy and mastectomy specimens. The images are taken using a microfocus x-ray tube and between 2 and 3 times geometric magnification and are recorded on a non-screen film system. These films are then digitized at 50-micron pixel resolution to produce a digital image with an effective pixel size of 25 microns for mastectomy specimens and 17 microns for biopsy specimens. Synthetic mammograms with actual lesions are created by segmenting the lesion from the biopsy image and adding them to the mastectomy image.

This approach has two distinct advantages. First, it can produce images unique to different types of detectors (e.g., digital versus screen-film systems or for different types of digital detectors). Second, it can produce images with true benign and malignant lesions, since the input specimens to the model will have known pathology. We illustrate the technique using phantom images.

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RADIOLOGIST EVALUATION OF DEI BREAST SPECIMEN IMAGING

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PURPOSE: The purpose of this study is to determine the potential utility of a new type of imaging method, Diffraction Enhanced Imaging, DEI. The long-term goal of this program is to develop a clinically-based DEI system for breast imaging. To accomplish this, we must identify the optimal DEI parameters for improved visualization of breast tissue structures and based on these parameters develop a conceptual design of a clinical DEI system. In order to standardize the statistical analysis, mammography phantoms will be used to simulate breast tissue.

METHODS AND MATERIALS: Breast imaging requires a high degree of spatial resolution to visualize abnormalities in the breast, such as calcifications, which can often be as small as 20-50 microns in diameter when clinically important. Two challenging phantoms designed to test the resolving ability of an imaging system were chosen for this study. In creating a DEI prototype, each component of the system can affect image quality. The following parameters were varied in the acquisition process: beam energy, analyzer crystal configuration, angle of the analyzer crystal, and crystal lattice plane. The specific parameter values must be known before we can design a "compact" machine. To determine which parameter values provide images of most use to readers, we performed a reader study where readers scored images taken at each of the parameter values according to which images yield the image information.

RESULTS: All images have been obtained from the National Synchrotron Light Source at Brookhaven National Labs and a reader study is currently underway using physicists and radiologists to test these parameters. DEI may eventually allow for visualization of breast abnormalities that can not be detected with conventional x-ray systems.

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INVESTIGATION OF POLYCAPILLARY X-RAY OPTICS FOR POTENTIAL APPLICATION FOR CLINICAL MONOCHROMATIC MAMMOGRAPHY

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Monochromatic imaging is typically done with synchrotron sources. These sources are expensive and not practical for clinical settings. However, conventional laboratory sources have insufficient intensity. Polycapillary x-ray optics can be used to efficiently produce an intense parallel beam, which can be diffracted from a crystal to create monochromatic radiation. Monochromatic parallel beam imaging produces high subject contrast, high resolution, and low patient dose.

Polycapillary collimating optics were investigated for their suitability for clinical use. Measurements of the optics included transmission, uniformity, and exit angle divergence. The transmission for a prototype with a 250-mm source to optic distance was 37 % at 17.5 keV, which matched well to the simulation. Field uniformity across the entire optic output was approximately 7 % rms. The output divergence from the optic was about 4 mrad, again in good agreement with simulation results.

Contrast, resolution, and intensity measurements were performed with both high and low angular acceptance crystals. Testing was first done at 8 keV with an intense copper rotating anode source. Preliminary 17.5 keV measurements were then made with a low power molybdenum source. At 8 keV, contrast enhancement was a factor of five relative to the polychromatic case, in good agreement with theoretical values. At 17.5 keV, monochromatic subject contrast was a factor of two times greater than the conventional polychromatic contrast. An additional factor of two increase in contrast is expected from the efficient removal of scatter by using the air gap which is allowable from the parallel beam. The measured angular resolution with a silicon crystal is 0.6 mrad at 8 keV, and 0.2-0.3 mrad at 17.5 keV. For a 50-mm thick patient, this angle corresponds to 50 lp/mm with an ideal detector. The use of polychromatic collimating optics allowed monochromatic imaging measurements using a conventional rotating anode source and computed radiography plate.

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IMPROVING IMAGING PERFORMANCE OF DIRECT FLAT-PANEL MAMMOGRAPHY DETECTORS FOR DIGITAL TOMOSYNTHESIS

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Currently, the only effective means of reducing mortality from breast cancer is through early detection, and x-ray mammography is the best method for detection of early stage breast malignancy. With the development of digital mammography, digital tomosynthesis has recently been proposed as a method to increase the accuracy of diagnosis. In tomosynthesis, a series of images are acquired with the x-rays entering at different angles to a stationary breast. By manipulating the digital images with a reconstruction algorithm, it is possible to reconstruct any plane in the breast that is parallel to the detector. This method allows the radiologist to see through the “structural noise” of surrounding breast tissue and make more accurate diagnosis. Tomosynthesis requires a sequence of images to be acquired very rapidly (several frames per second), each of which free from temporal artifacts (lag and ghosting), and x-ray quantum noise limited at a fraction (1/10 or less) of the dose of a standard single view mammogram. This is a tremendous challenge for the development of digital mammography detectors. The objectives of the our project is to demonstrate that the imaging performance of an amorphous selenium flat-panel digital mammography detector can be optimized for low dose and high frame rate in order to generate high quality tomosynthetic images. For the present work, we used theoretical models and individual a-Se samples to study the x-ray sensitivity and temporal imaging performance (lag and ghosting) as a function of detector design and operational conditions so that they can be optimized for low dose and high frame rate. The results showed that the x-ray sensitivity of a-Se can be increased by 50 % by doubling the electric field, which is important for low dose performance. In order for the detector to operate at high frame rate without artifact, a preconditioning process is desirable where the detector is exposed uniformly to visible light in order for charge to build up in the gap between pixel electrodes so that the pixel fill-factor is unity across the entire detector. Our work will improve the image quality of digital tomosynthetic mammograms, which can minimize breast structural noise and potentially improve breast cancer detection and diagnosis.

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